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| EXAMINER | |
|---|---|
| BARTON, JEFFREY THOMAS | |
| **ART UNIT** | **PAPER NUMBER** |
| 1753 | |

DATE MAILED: 03/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/783,564 | MCGOWN, LINDA B. | |
| | Examiner | Art Unit | |
| | Jeffrey T. Barton | 1753 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20050307, 20041202*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Claim Rejections - 35 USC § 103*

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1, 10, 11, 13, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muscate et al in view of Rehder et al.

Relevant to claims 1, 10 and 11, Muscate et al disclose a capillary electrophoresis column comprising a matrix comprising a gel comprising a receptor oligonucleotide (Page 16, line 5 - Page 17, line 3; Page 11, line 19 - Page 12, line 10), wherein the gel comprises a monolithic form. (Page 13, line 18 - Page 15, line 19) This matrix and column would also be suitable for electrochromatography.

Relevant to claims 13 and 14, Muscate et al disclose a method for isolating an analyte from a mixture, the method comprising: contacting the mixture with a matrix comprising a monolithic gel comprising a receptor oligonucleotide (Page 19, lines 16-22), followed by elution of the target analyte from the matrix. (Page 20, lines 7-16; Page 13, line 18 - Page 15, line 19)

Muscate et al do not explicitly disclose the use of a receptor oligonucleotide that comprises a g-quartet-forming oligonucleotide.

Rehder et al disclose a capillary electrochromatographic device that uses immobilized g-quartet-forming oligonucleotides as receptors in the stationary phase, and would be suitable for use in an electrophoretic method. (Sections 1 and 2).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device and method of Muscate et al by replacing their gel-bound receptor oligonucleotide with a g-quartet-forming receptor oligonucleotide, as taught by Rehder et al, because Rehder et al teach their suitability for protein separations, given their weak, nondenaturing interactions with amino-acid based structures. (Page 3760, 2nd column, 1st full paragraph)

4. Claims 2 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muscate et al and Rehder et al as applied to claim 1 above, and further in view of Knapp et al.

Muscate et al and Rehder et al disclose a combination as described above for claims 1 and 13.

Neither Muscate et al nor Rehder et al explicitly disclose the matrix being disposed in a microfluidic device.

Knapp et al disclose a microfluidic device (500, Figure 5a) that comprises receptor oligonucleotides immobilized on a solid support or the capillary walls (At sites 506, 508, and 510; Column 32, lines 45-54)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of Muscate et al, Rehder et al, and Abrams et al by disposing their electrophoretic separation matrix in a microfluidic device, as taught by Knapp et al, because Knapp et al teach the usefulness of microfluidic devices in increasing throughput of analyses. (Column 1, line 66 - Column 2, line 20

5. Claims 3, 12, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muscate et al and Rehder et al as applied to claims 1, 10, and 13 above, and further in view of Weir et al and Abrams et al.

Muscate et al and Rehder et al disclose combination as described above for claims 1, 10, and 13. Muscate et al also disclose the ability to provide an electrophoresis capillary with plural zones containing gels of different characteristics (Page 16, lines 22-27)

Neither Muscate et al nor Rehder et al disclose the matrix further comprising an enzyme.

Weir et al disclose enzymatic lysis of a cell in order to obtain cell components for analysis. (Paragraph 0030)

Abrams et al disclose the immobilization of enzymes within their separation matrix (Column 8, lines 27-32)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of Muscate et al and Rehder et al, by binding a lysing enzyme to the separation matrix in the region upstream from the receptor oligonucleotides, as taught by Abrams et al and suggested by Weir et al, because it would allow direct analysis of microbial samples, without prior lysis.

6. Claims 4-8 and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muscate et al in view of Rehder et al and Abrams et al. Additional evidence relevant to claim 8 is given by Knobel.

Relevant to claims 4-8, Muscate et al disclose a capillary electrophoresis matrix comprising a gel comprising a receptor oligonucleotide (Page 16, line 5 - Page 17, line 3; Page 11, line 19 - Page 12, line 10), wherein the gel comprises a monolithic form. (Page 13, line 18 - Page 15, line 19) This matrix and column would also be suitable for electrochromatography.

Relevant to claims 16-19, Muscate et al disclose a method for isolating an analyte from a mixture, the method comprising: contacting the mixture with a matrix comprising a gel comprising a receptor oligonucleotide (Page 19, lines 16-22), followed by elution of the target analyte from the matrix. (Page 20, lines 7-16)

Muscate et al do not explicitly disclose the use of a receptor oligonucleotide that comprises a g-quartet-forming oligonucleotide. They also do not disclose the use of beads embedded in a gel comprising a g-quartet-forming oligonucleotides (Claims 4 and 16), wherein the beads are chromatography packing beads (Claims 5 and 17), wherein the beads are functionalized (Claims 6 and 18), or wherein the beads are functionalized with a protein, oligonucleotides, or combination thereof. (Claims 7 and 19) They also do not explicitly disclose beads embedded in a monolithic gel. (Claim 8)

Rehder et al disclose a capillary electrochromatographic device that uses immobilized g-quartet-forming oligonucleotides as receptors in the stationary phase, and would be suitable for use in an electrophoretic method. (Sections 1 and 2).

Abrams et al disclose the use of beads embedded in a gel comprising affinity ligands (Column 8, lines 56-63), wherein the beads are chromatography packing beads (Column 8, lines 34-37 and 56-63), wherein the beads are functionalized (Column 8, lines 34-37 and 56-63), or wherein the beads are functionalized with a protein, oligonucleotides, or combination thereof. (Column 8, lines 27-37 and 56-63)

Abrams et al also reference Knobel in describing a method of suspending particles in a gel. (Column 8, lines 60-61) This method will result in formation of a monolithic gel.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device and method of Muscate et al by replacing their gel-bound receptor oligonucleotide with a g-quartet-forming receptor oligonucleotide, as taught by Rehder et al, because Rehder et al teach their suitability for protein

separations, given their weak, nondenaturing interactions with amino-acid based structures. (Page 3760, 2nd column, 1st full paragraph)

It would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combinations of Muscate et al and Rehder et al by incorporating oligonucleotide-functionalized chromatography packing beads into the gel, as taught by Abrams et al, because it would allow convenient incorporation of affinity ligands for different analytes.

7. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Muscate et al, Rehder et al, and Abrams et al as applied to claim 4 above, and further in view of Knapp et al.

Muscate et al, Rehder et al, and Abrams et al disclose a combination as described above for claim 4.

None among Muscate et al, Rehder et al, and Abrams et al disclose the matrix being disposed on a microfluidic device.

Knapp et al disclose a microfluidic device (500, Figure 5a) that comprises receptor oligonucleotides immobilized on a solid support or the capillary walls (At sites 506, 508, and 510; Column 32, lines 45-54)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of Muscate et al, Rehder et al, and Abrams et al by disposing their electrophoretic separation matrix in a microfluidic device, as taught by Knapp et al, because Knapp et al teach the usefulness of

microfluidic devices in increasing throughput of analyses. (Column 1, line 66 - Column 2, line 20

8. Claims 21-23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muscate et al in view of Rehder et al and Weir et al.

Relevant to claim 21, Muscate et al disclose a method for isolating an analyte from a mixture, the method comprising: contacting the mixture with a matrix comprising a gel comprising a receptor oligonucleotide (Page 19, lines 16-22), followed by washing the matrix to remove non-bound material. (Page 20, lines 1-5)

Relevant to claim 23, Muscate et al disclose the use of a monolithic gel. (Page 13, line 18 - Page 15, line 19)

Muscate et al do not explicitly disclose the use of a receptor oligonucleotide that comprises a g-quartet-forming oligonucleotide, nor do they disclose detection of the analyte bound to the matrix.

Rehder et al disclose a capillary electrochromatographic method that uses immobilized g-quartet-forming oligonucleotides as receptors in the stationary phase, and would be suitable for use in an electrophoretic method. (Sections 1 and 2).

Relevant to claim 21, Weir et al disclose detection of analytes bound by receptor oligonucleotides immobilized within the matrix. (Paragraph 0080)

Relevant to claim 22, Weir et al disclose the target analyte being a nucleic acid present within the genome of a microbe (Paragraph 0030)

Relevant to claim 25, Weir et al disclose lysis of a cell that comprises the target analyte. (Paragraph 0030)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Muscate et al by replacing their gel-bound receptor oligonucleotide with a g-quartet-forming receptor oligonucleotide, as taught by Rehder et al, because Rehder et al teach their suitability for protein separations, given their weak, nondenaturing interactions with amino-acid based structures. (Page 3760, 2nd column, 1st full paragraph)

It would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of Muscate et al and Rehder et al by incorporating a detector for detection of analytes bound by the receptor oligonucleotides, as taught by Weir et al, because it would provide information on binding status during the analysis procedure, and thus aid in identifying analytes and/or their concentration. The value of such information would be readily apparent to a skilled artisan.

Addressing claims 22 and 25, it would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of Muscate et al and Rehder et al by analyzing nucleic acids within the genome of a microbe that had previously undergone lysis, as also taught by Weir et al, because it would provide greater genetic understanding of the microbe. Such selection of a particular sample to be analyzed lies within the level of ordinary skill in the art.

9. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over Muscate et al, Rehder et al, and Weir et al as applied to claim 21 above, and further in view of Abrams et al.

Muscate et al, Rehder et al, and Weir et al disclose a combination as described above for claim 21. Muscate et al also disclose the ability to provide an electrophoresis capillary with plural zones containing gels of different characteristics. (Page 16, lines 22-27) Weir et al also disclose enzymatic lysis of a cell in order to obtain the nucleic acids for analysis. (Paragraph 0030)

None among Muscate et al, Rehder et al, and Weir et al disclose the matrix further comprising an enzyme.

Abrams et al disclose the immobilization of enzymes within their separation matrix (Column 8, lines 27-32)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of Muscate et al and Rehder et al, and Weir et al, by binding an lysing enzyme to the separation matrix in the region upstream from the receptor oligonucleotides, as taught by Abrams et al and suggested by Weir et al, because it would allow direct analysis of microbial samples, without prior lysis.

10. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Muscate et al, Rehder et al, and Weir et al as applied to claim 21 above, and further in view of Knapp et al.

Muscate et al, Rehder et al, and Weir et al disclose a combination as described above for claim 21.

None among Muscate et al, Rehder et al, and Weir et al disclose the matrix being disposed on a microfluidic device.

Knapp et al disclose a microfluidic device (500, Figure 5a) that comprises receptor oligonucleotides immobilized on a solid support or the capillary walls (At sites 506, 508, and 510; Column 32, lines 45-54)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of Muscate et al, Rehder et al, and Weir et al by disposing their electrophoretic separation matrix on a microfluidic device, as taught by Knapp et al, because Knapp et al teach the usefulness of microfluidic devices in increasing throughput of analyses. (Column 1, line 66 - Column 2, line 20

11. Claims 2, 15, and 27-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knapp et al in view of Muscate et al and Rehder et al.

Relevant to all claims, Knapp et al disclose a microfluidic device (500, Figure 5a) that comprises receptor oligonucleotides immobilized on a solid support or the capillary walls (At sites 506, 508, and 510; Column 32, lines 45-54)

Relevant to claim 15, Knapp et al disclose a method of isolating an analyte from a mixture, the method comprising: contacting a sample mixture with a matrix comprising a receptor oligonucleotide, followed by eluting the target analyte from the matrix. (Column 32, line 24 - Column 34, line 56)

Relevant to claims 28 and 31, Knapp et al disclose receptor oligonucleotides disposed in a channel of the device (Column 32, lines 43-48)

Relevant to claim 29, Knapp et al disclose a microfluidic system suitable for multiple processes according to their invention (See Figure 11; Column 49, line 41 - Column 50, line 28)

Relevant to claim 30, Knapp et al disclose a method for transporting reagents on a microfluidic device comprising: providing the microfluidic device described above, contacting the device with reagent (Figure 5a; Column 32, lines 24-25), and applying a force to transport the reagent. (Column 50, line 51 - Column 51, line 51)

Relevant to claim 32, Knapp et al disclose the motion-causing force being supplied by a pump or electrical current (Column 50, line 51 - Column 51, line 51)

Relevant to claim 33, Knapp et al disclose the reagent being a nucleic acid molecule (Column 32, lines 24-27)

Knapp et al do not explicitly disclose the use of a receptor oligonucleotide that comprises a g-quartet-forming oligonucleotide. (All claims) They also do not specifically disclose a gel comprising a g-quartet-forming oligonucleotide. (Claims 2 and 15)

Muscate et al disclose a capillary electrophoresis matrix comprising a gel comprising a receptor oligonucleotide (Page 11, line 19 - Page 12, line 10)

Rehder et al disclose a capillary electrochromatographic device that uses immobilized g-quartet-forming oligonucleotides as receptors in the stationary phase, and would be suitable for use in an electrophoretic method. (Sections 1 and 2).

The obvious combination of Muscate et al and Rehder et al was discussed above.

It would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Knapp et al by replacing their solid-supported receptor oligonucleotides with a gel that comprises a g-quartet-forming receptor oligonucleotides, as taught by the combination of Muscate and Rehder, because Rehder et al teach their suitability for protein separations, given their weak, nondenaturing interactions with amino-acid based structures. (Page 3760, 2nd column, 1st full paragraph) and because Knapp et al disclose a broad spectrum of potential analytes, including proteins (Column 8, lines 12-16), the separation of which would be facilitated by the g-quartets taught by Rehder et al.

***Conclusion***

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

JTB
March 24, 2005

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